

In the Specification:

On page 1, delete lines 6 through 9 and substitute This application is a Divisional application of

U.S. Serial No. 08/660,697, filed June 5, 1996, entitled *Structurally Determined Metallo-Constructs and Applications*, the teachings of which are incorporated herein by reference as if set forth in full.—

In the Claims:

Please cancel claims 1 through 34.

Please add the following new claims:

41. A combinatorial library of different sequence peptide or peptidomimetic members synthesized on solid phase, where each constituent library member comprises:
- a sequence of three or more amino acid residues, mimics of amino acid residues or combinations thereof, bound to solid phase characterized by (i) a sequence of two or more amino acid residues, mimics of amino acid residues or combinations thereof, forming a metal ion-binding domain, (ii) a sequence of one or more amino acid residues, mimics of amino acid residues or combinations thereof, at the N- or C- terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain, and (iii) a cleavable bond attaching the sequence to solid phase; and
 - a unique selection or sequence of amino acid residues, mimics of amino acid residues or combinations thereof.
42. The combinatorial library of claim 41 wherein the metal ion-binding domain further comprises at least one residue with at least one sulfur available for binding to a metal ion.
43. The combinatorial library of claim 42 wherein the metal ion-binding domain further comprises at least one residue with at least one nitrogen available for binding to a metal ion.
44. The combinatorial library of claim 42 wherein the metal ion-binding domain comprises three residues forming an N_3S_1 metal ion complexation group.

Sulf
S-2-Cmt

45. The combinatorial library of claim 42 wherein the at least one sulfur is protected by a removable S-protecting group.

46. The combinatorial library of claim 45 wherein the removable S-protecting group is Trt.

47. The combinatorial library of claim 41 wherein the diversity in the sequence occurs in the metal ion-binding domain.

48. The combinatorial library of claim 41 wherein the diversity in the sequence occurs outside the metal ion-binding domain.

49. The solid phase combinatorial library of claim 42 wherein the at least one residue containing at least one sulfur available for binding to a metal ion is L- or D-cysteine; L- or D-penicillamine; L- or D-homocysteine; 2'-mercapto-tryptophan; N^B-(2 mercaptoethane)-α,β-diaminopropionic acid; 2-mercaptoethylamine; thioglycolic acid; mercaptopropionic acid; 2-mercaptoaniline; or 2-mercaptosuccinic acid.

50. A combinatorial library of different sequence peptide or peptidomimetic members synthesized in solution, where each constituent library member comprises:

(a) a sequence of a combination of three or more amino acid residues and mimics of amino acid residues characterized by (i) a sequence of two or more amino acid residues, mimics of amino acid residues or combinations thereof forming a metal ion-binding domain, and (ii) a sequence of one or more amino acid residues, mimics of amino acid residues or combinations thereof at the N- or C- terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain; and

(b) a unique selection or sequence of amino acid residues, mimics of amino acid residues or combinations thereof.

51. The combinatorial library of claim 50 wherein the metal ion-binding domain further comprises at least one residue with at least one sulfur available for binding to a metal ion.

Sulf
C3

52. The combinatorial library of claim 51 wherein the metal ion-binding domain further comprises at least one residue with at least one nitrogen available for binding to a metal ion.

53. The combinatorial library of claim 52 wherein the metal ion-binding domain comprises three residues forming an N₃S₁ metal ion complexation group.

54. The combinatorial library of claim 50 wherein the at least one sulfur is protected by a removable S-protecting group.

55. The combinatorial library of claim 54 wherein the removable S-protecting group is Trt.

56. The combinatorial library of claim 50 wherein the diversity in the sequence occurs in the metal ion-binding domain.

57. The combinatorial library of claim 50 wherein the diversity in the sequence occurs outside the metal ion-binding domain.

58. The combinatorial library of claim 51 wherein the at least one residue containing at least one sulfur available for binding to a metal ion is L- or D-cysteine; L- or D-penicillamine; L- or D-homocysteine; 2'-mercapto-tryptophan; N⁸-(2 mercaptoethane)-α,β-diaminopropionic acid; 2-mercaptoethylamine; thioglycolic acid; mercaptopropionic acid; 2-mercaptoaniline; or 2-mercaptosuccinic acid.

59. The combinatorial library of claim 50 wherein each constituent library member further comprises a metal ion complexed to the metal ion-binding domain.

60. A method for generating a metallopeptide or metallopeptidomimetic combinatorial library, comprising the steps of:

(a) constructing a library containing a plurality of sequences of the formula R₁-X-R₂ cleavably bound to solid phase, wherein

(i) X comprises at least two amino acid residues, mimics of amino acid residues or combinations thereof, with at least one of said residues comprising at least one nitrogen atom available to complex with the coordination sphere of a metal ion, the metal ion to be provided, and with at least one of said residues comprising at least one sulfur atom available to complex with the coordination sphere of a metal ion, the metal ion to be provided;

(ii) R₁ and R₂ each comprise from 0 to about 20 amino acid residues, mimics of amino acid residues or combinations thereof, provided that R₁ and R₂ comprise at least 1 amino acid residue or mimic of an amino acid residue, and provided that between at least two of the plurality of sequences of the formula R₁-X-R₂ at least either R₁ or R₂ differ in at least either the sequence of residues or the selection of residues;

(b) complexing a metal ion to X;

wherein the resulting metal ion-complexed sequences form a metallopeptide or metallopeptidomimetic combinatorial library.

61. The method of claim 60 wherein at least one of said residues comprising at least one sulfur atom is L- or D-cysteine; L- or D-penicillamine; L- or D-homocysteine; 2'-mercapto-tryptophan; N^B-(2 mercaptoethane)-α,β-diaminopropionic acid; 2-mercaptopethylamine; thioglycolic acid; mercaptopropionic acid; 2-mercptoaniline; or 2-mercaptosuccinic acid.

62. The method of claim 60 wherein X comprises three residues forming an N₃S₁ metal ion complexation group.—

REMARKS

This preliminary amendment is being filed concurrently with a 37 CFR 1.56(b) Divisional Patent Application Transmittal and the amendments are directed thereto. No new matter is believed to be introduced. Entry of this amendment by the Examiner is respectfully requested.